REMARKS

Applicants thank the Examiner for meeting with Applicants' representatives on June 10, 2004, to discuss the pending rejections and strategies for amending the claims so as to create allowable subject matter in this application.

Applicants herein cancel claims 23 and 24 without prejudice, amend claims 1, 2, 20, 25, and 26, and add new claims 28-57. Applicants amend the claims to include methods described in the specification and to more clearly claim the invention by recitation of particular conditions and, in certain instances, requiring the identification of a subject at risk of thrombosis. Applicants submit that the amendments do not introduce new matter. Specifically, exemplary support for amendments to the claims is in the specification at page 6, lines 26-31 (P-selectin ligand activity), page 7, line 28 to page 8, line 12 (specific conditions associated with thrombosis, prophylactic treatment), page 9, lines 22-32 (PSGL-1), page 36, lines 24-27 (prophylactic treatment), and page 37, line 18 to page 38, line 10 (specific conditions), for example.

The previously pending claims were rejected on novelty and obviousness grounds. As amended, claim 1 now lists specific disorders, conditions, or procedures that are neither taught nor suggested by the prior art. Independent claims 25 and 57 list the specific disorders, conditions, and procedures of amended claim 1 and additionally require identifying a subject at risk of thrombosis. New claim 31 relates to treatment of deep vein thrombosis, a disorder that is not disclosed or suggested by the prior art. Claims 40-44, depending from claim 31, recite the specific indications of claim 1. And finally, new claim 45 recites a prophylactic method of treating thrombosis, requiring

identification of a subject at risk of thrombosis and administration of a soluble PSGL-1 protein. This claim is also introduced with dependent claims drawn to the specific indications of amended claim 1. Applicants believe that this amendment places the claims in condition for allowance.

Anticipation by Cummings et al. (U.S. Patent No. 5,464,778)

Previously pending claims 1-4, 8-13, 16-18, and 23-27 were rejected as anticipated under 35 U.S.C. § 102(e) by Cummings et al., U.S. Patent No. 5,464,778.

In the Final Office Action, the Examiner states that Cummings discloses the use of PSGL in the treatment of acute and chronic conditions associated with leukocyte adherence, inflammation, and coagulation, including ischemia-reperfusion injury and atherosclerosis. The Examiner argues that the inhibition of thrombosis is a therapeutic effect of the disclosed treatment of clinical disorders including ischemia reperfusion injury, coagulation diseases, and atherosclerosis. The Examiner states that these disorders are associated with therapeutic endpoints that include the inhibition of thrombosis.

The Examiner recognizes that the PSGL-1 proteins of claims 5, 6, 14, and 15 comprising an immunoglobulin sequence, are not disclosed in Cummings, but alleges that other claimed structural limitations of PSGL-1 (for example, SEQ ID NO:2 and active fragments thereof) are inherently disclosed by isolation and partial purification of PSGL-1 in Cummings. The Examiner further alleges that claimed functional limitations are inherently disclosed in Cummings, and thus the claims are anticipated and obvious

over the prior art. Applicants disagree. Nevertheless, Applicants have amended the claims to recite additional limitations not taught by the prior art.

Cummings does not teach the use of PSGL-1 to treat the specific disorders, conditions, or procedures of amended claims 1, 25, 28-30, 40-44, 46-49 and 57 and their respective dependent claims. Disclosure of the use of PSGL-1 to treat ischemia reperfusion injury, coagulation, or atherosclerosis does not anticipate or render obvious its use to treat any of the indications added by amendment to claim 1. Thus, the disorders of Cummings are not related to the newly recited disorders in claim 1, such as atrial fibrillation or arrhythmia. Cummings does not describe the use of PSGL-1 to treat non-mobile individuals, or those undergoing surgical or vascular procedures. Deep vein thrombosis, including DVT relating to surgical intervention, bed rest, or prolonged sitting, is similarly novel and inventive over Cummings, which merely discloses coagulation disorders such as disseminated intravascular coagulation, bacterial sepsis, or circulatory shock.

Further, Cummings does not teach use of PSGL-1 in a subject that is identified as at risk of thrombosis. As Cummings discloses a use of PSGL-1 to treat certain conditions that are associated with PSGL-1, and despite the Examiner's allegation that given the "nature" of acute or chronic thrombotic conditions, one of ordinary skill in the art would provide PSGL prior to thrombus formation (Office Action at page 4), mere mention of use in a non-specified "chronic" disorder, see column 18, lines 50-52, does not imply or inherently disclose prevention or prophylactic treatment of thrombosis.

Nor does Cummings disclose or suggest the PSGL-1 fragments and sequences of claims 9-14, as the Examiner recognizes at page 7 of the Final Office Action. Thus,

the particular conditions and procedures claimed, the treatment of deep vein thrombosis, and prophylactic administration of PSGL-1 to prevent thrombosis in a subject at risk of thrombosis are novel and non-obvious over Cummings. Applicants request that the Examiner withdraw this rejection.

Anticipation by Larsen et al. (U.S. Patent No. 5,840,679)

Similarly, the rejection of the previously pending claims 1-5, 7-18, and 23-27 under 35 U.S.C. § 102(e) as anticipated by Larsen et al. (U.S. Patent No. 5,840,679) is not applicable to the amended claims for the reasons stated above.

Larsen is cited by the Examiner for teaching the use of PSGL and its fragments to treat conditions characterized by P-selectin mediated intercellular adhesion, such as myocardial infarction. The Examiner states that Larsen also discloses the combination of PSGL "with other pharmaceutical compositions, including anti-inflammatory and thrombolytic or anti-thrombotic agents." The Examiner alleges that the claims include underlying mechanisms or physiology that contribute to thrombosis, but do not appear to distinguish prior art teaching the same or nearly the same methods to achieve the same or nearly the same effect. As with the rejection over Cummings, the Examiner argues that the structural and functional limitations of the claims are inherently anticipated by Larsen. Applicants have previously argued over this rejection, and without acquiescing, now amend the claims solely in an effort to facilitate prosecution.

Larsen does not teach the use of PSGL-1 to treat the specific disorders, conditions, or procedures of the amended claims. The particular conditions of the amended claims are novel over Larsen's disclosure of <u>different</u> disorders that are

characterized by PSGL-1's effect on inflammation. One of ordinary skill would not extrapolate from the disclosure of Larsen to be motivated to treat or expect success in treating the specific disorders of the amended claims. For example, disclosure of a use of PSGL-1 to treat myocardial infarction does not anticipate or render obvious PSGL-1's use to treat hypertension or aortic bending. Larsen also does not describe the identification of individuals at risk of thrombosis, and it does not teach prevention and prophylactic use of PSGL-1 in a subject that is identified as at risk of thrombosis. The use of PSGL-1 in non-mobile individuals or those undergoing surgical or vascular procedures is similarly not disclosed. Deep vein thrombosis, including DVT relating to surgical intervention, bed rest, or prolonged sitting, is further not described or suggested by Larsen.

Applicants request that the Examiner withdraw this rejection.

Obviousness over Cummings and Larsen in view of Maugeri and/or Johnson

The Examiner also has rejected all previously pending claims under 35 U.S.C. § 103 over the combination of Cummings and Larsen with either Maugeri or Johnston. The Examiner states that Cummings and Larsen do not disclose the role of LTC_4 in thrombus formation and thrombotic conditions per se, but that LTC_4 was a known thrombus-inducing agent in thrombus formation and thrombotic conditions. The Examiner alleges that Maugeri and/or Johnston provide that knowledge, and asserts that Maugeri and Johnston each teach the role of LTC_4 in leukocyte adhesion and the ability of P-selectin antagonists to inhibit leukocyte adhesion.

Both Maugeri and Johnson describe a mechanistic link between P-selectin and LTC_4. The Examiner postulates that LTC_4 was a known thrombus-inducing agent, and that the description of reduced production of LTC_4 (Maugeri) or inhibition of LTC_4-induced leukocyte rolling (Johnson) with the administration of an antibody to P-selectin would motivate a skilled artisan to administer PSGL-1 to treat patients with various thrombotic conditions. In contrast, Maugeri discloses that LTC_4 is a vascoconstrictor, and Johnson discloses the use of LTC_4 to induce an "acute" experimental model of inflammation. These references do not disclose a thrombotic effect of P-selectin, let alone a thrombotic effect of PSGL-1. Applicants have previously argued against this rejection and believe it is improper; nevertheless, Applicants now amend the claims in an effort to facilitate prosecution.

As discussed above, Larsen and Cummings do not provide or suggest the specific disorders, conditions, and procedures of the amended claims, the identification of a subject at risk of thrombosis, or prophylactic methods relating to thrombosis. Maugeri and Johnson do not compensate for this deficiency as neither discuss the specific disorders, conditions, and procedures of the amended claims, the identification of a subject, or prevention of thrombosis. Additionally, Maugeri and Johnson do not disclose PSGL-1 antagonists, their use, or a role for PSGL-1 in the treatment of any disease.

Therefore, the obviousness rejections combining Cummings and Larsen with these references should accordingly be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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